

CLAIMS

We claim:

1. A method for predicting the response of a patient with chronic lymphocytic leukemia to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes and activates the complement cascade and immune effector cells in the patient, thereby depleting B lymphocytes from the patient's peripheral blood, lymph nodes and bone marrow, comprising:

collecting from the patient a cell sample; and

analyzing the cell sample to detect one or more cytogenetic abnormalities selected from

10 the group consisting of del(17p13.1), del(13q14.3), del(11q22-q23) and trisomy 12;

wherein the presence of the del(17p13.1) abnormality is indicative that the patient will be refractory to treatment with said agent, and wherein the absence of the del(17p13.1) abnormality together with the presence of one or more of the del(13q14.3), del(11q22-q23) and trisomy 12 abnormalities is indicative that the patient will be responsive to treatment with said agent.

15 2. The method of claim 1 wherein the therapeutic agent is rituximab.

3. The method of claim 1 wherein the cell sample comprises B lymphocytes.

4. The method of claim 1 wherein analysis of the cell sample uses polynucleotide probes and fluorescence in situ hybridization (FISH).

5. The method of claim 4 wherein the FISH uses the LSI p53 probe to detect del(17p13.1).

20 6. The method of claim 4 wherein the FISH uses the LSI D13S319 probe to detect del(13q14.3).

7. The method of claim 4 wherein the FISH uses the CEP 12 probe to detect trisomy 12.

8. The method of claim 4 wherein the FISH uses the ATM probe to detect del(11q22.3).

9. A diagnostic kit for determining the chemosensitivity of a chronic lymphocytic leukemia patient to treatment with a therapeutic agent that is specific for CD20+ B lymphocytes, comprising:

one or more polynucleotide probes, each of which comprises a polynucleotide sequence which is complementary to and hybridizes under stringent conditions with a target region of chromosomal DNA in a human

wherein one of the probes is complementary to and hybridizes under stringent conditions with
5 the target region 17p13.1 of chromosome 17, and wherein the other probes are complementary to and hybridize under stringent conditions with the target regions selected from the group consisting of the 13q14.3 region of chromosome 13, the 12p11.1-q11 region of chromosome 12, and the 11q22.3 region of chromosome 12.

10. The kit of claim 9 wherein the probes comprise polynucleotides from 50 to 10^5 nucleotides in length.

11. The kit of claim 10 wherein the probes are selected from the group consisting of oligonucleotides, cDNA molecules, RNA molecules, and synthetic gene probes comprising nucleobases.

12. The kit of claim 9, wherein the probe for the target region 17p13.1 of chromosome 17 is the
15 LSI p53 probe, the probe for the 13q14.3 region of chromosome 13 is the LSI D13S319 probe, the probe for the 12p11.1-q11 region of chromosome 12 is the CEP 12 probe, and the probe for the 11q22.3 region of chromosome 11 is the ATM probe.

13. A method of identifying a patient as likely to be refractory to treatment with rituximab, comprising;

20 analyzing the genome of cells obtained from the patient for the presence of del(17p13.1),

wherein presence of del(17p13.1) indicates that the patient is likely to be refractory to treatment with rituximab.

25 14. The method of claim 13 wherein analysis of the genome uses fluorescence in situ hybridization (FISH).

15. The method of claim 14 wherein the FISH uses the LSI p53 probe.

16. A method of identifying a patient as likely to respond to treatment with rituximab, comprising;

analyzing the genome of cells obtained from the patient for the presence of del(17p13.1), and one or more of del(13q14.3), del(11q22.3) and trisomy 12,

wherein absence of del(17p13.1) and presence of one or more of del(13q14.3), del(11q22.3) or trisomy 12, indicates the patient is likely to respond to treatment with rituximab.

5 17. The method of claim 16 wherein analysis of the genome uses fluorescence in situ hybridization (FISH).

18. The method of claim 17 wherein the FISH uses the LSI p53 probe to detect del(17p13.1).

19. The method of claim 17 wherein the FISH uses the LSI D13S319 probe to detect del(13q14.3).

10 20. The method of claim 17 wherein the FISH uses the CEP 12 probe to detect trisomy 12.

21. The method of claim 17 wherein the FISH uses an approximately 500 kb probe that hybridizes to a locus from D11S1828-D11S1294 to detect del(11q22.3), wherein the probe includes a portion that hybridizes with the Ataxia telangiectasia mutated (“ATM”) gene.

22. The method of claim 21 wherein the 500 kb probe is designated as ATM.

15 23. A method for predicting the response of a patient with chronic lymphocytic leukemia to treatment with a therapeutic agent that specifically binds to CD52 antigens on the surface of B-lymphocytes and activates the complement cascade and immune effector cells in the patient, thereby depleting B lymphocytes from the patient’s peripheral blood, lymph nodes and bone marrow, comprising, comprising:

20 collecting from the patient a cell sample; and

analyzing the cell sample to detect the cytogenetic abnormality del(17p13.1),

wherein the presence of the del(17p13.1) abnormality is indicative that the patient will be responsive to treatment with the agent.

24. The method of claim 23 wherein the therapeutic agent is alemtuzumab.

25 25. The method of claim 23 wherein the cell sample comprises B lymphocytes.

26. The method of claim 23 wherein analysis of the cell sample uses polynucleotide probes and fluorescence in situ hybridization (FISH).

27. The method of claim 26 wherein the FISH uses the LSI p53 probe to detect del(17p13.1).
28. A method of identifying a patient as likely to respond to treatment with alemtuzumab, comprising:
 - analyzing the genome of cells obtained from the patient for the presence of
5 del(17p13.1),
 - wherein the presence of del(17p13.1) indicates the patient is likely to respond to treatment with alemtuzumab.
29. The method of claim 28 wherein analysis of the genome uses fluorescence in situ hybridization (FISH).
- 10 30. The method of claim 29 wherein the FISH uses the LSI p53 probe to detect del(17p13.1).